-- 39. (New) A method according to Claim 24, wherein said period of time is up to 100 days.

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40. (New) A method according to Claim 31, wherein said cells are cultivated for a period of time up to 100 days.

41. (New) A method according to Claim 36, wherein said transplanted cells persist in said mammal for a period of time up to 100 days. --

Remarks

A Notice of Appeal with the requisite fees was mailed on April 2, 2003.

Careful consideration has been given to the Advisory Action of April 24, 2003. Reconsideration of the application in view of the above amendments and the following remarks is respectfully requested.

New claims 39-41 have been introduced to round out the scope of protection for the invention to which the Applicants should be entitled. The additional claims define more specific features of the invention as set forth in paragraphs 2-4 of page 4 of the specification.

The Advisory Action established in response to the Amendment After Final Rejection, mailed on February 10, 2003, maintains the rejection of claims 19-38 under 35 U.S.C. 112, first paragraph, allegedly, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with

which it is most nearly connected, to make and/or use the invention.

In the Office Action of February 13, 2002, it is stated that "The specification does not disclose how to make a polyacrylamide gel that would persist for a length of time in vivo and not result in a non-specific inflammatory response...Given the state of the art which teaches against the use of polyacrylamide that has not been completely eliminated of toxic substances, and the lack of teachings in the specificaiton regarding a specific polyacrylamide gel formulation that would function as claimed, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the claimed invention."

In Applicants' response mailed June 10, 2002, it was argued that, prior to the filing date of this application, it was known by those skilled in the art to employ polyacrylamide gel for medical purposes, such as for plastic surgery. With the response, Applicants submitted, for the Examiner's consideration, a copy of a Russian patent (RU2127129), together with an English translation of relevant portions of that document. The patent, dealing with a process for production of gel-like material containing polyacrylamide gel, discloses, on page 4, a heating process for eliminating toxic material, i.e. acrylamide monomers, from the polymer produced, so as to minimize any inflammatory reaction which may be caused by the presence of the monomers when the polyacrylamide gel is used for soft tissue plastic surgery.

Nevertheless, in the Office Action of October 2, 2002, the rejection of the claims was maintained on the ground that incorporation of essential material into the specification by reference to a foreign application or patent, or to a publication, is improper.

In response to the Office Action, Applicants argued that, by submission of the foreign document, they were not seeking to incorporate any subject matter into the specification but intended only to establish that one skilled in the art, at the time the subject application was filed, knew how to produce polyacrylamide gel for medical uses so that description in the specification of such process(es) should not be required and would in fact be superfluous. Applicants made reference to MPEP 2164.05(a) wherein it is stated that: "The specification need not disclose what is well-known to those skilled in the art and preferably omits that

which is well-known to those skilled and already available to the public." Applicants submitted copies of additional publications to show that those skilled in the art knew of and were using medical grade polyacrylamide gel, e.g. Formacryl, prior to the filing date of the subject application.

Notwithstanding the submission of the above proofs, the Advisory Action of April 24, 2003 maintained the rejection of the claims for the reasons of record. The action states that "The translated priority document indicates that the polyacrylamide used in the instant invention was made by a process which includes the heating of the polymerized gel to 100 or 105 degrees centigrade after the normal time allotted for polymerization. This heating step appears to be novel in the art and would be expected to rid the polymerized gel of monomer by subjecting said gel to a higher temperature than that which is taught in the art. However, this limitation is not taught by any of the aforesaid patents nor mentioned in the text from the BioForm Research Center provided with the response."

The Examiner appears to contend that it is not sufficient to have provided one prior art document to show that the skilled person was already familiar with preparing medical grade polyacrylamide gel which could be used in carrying out the subject invention, but that other documents submitted also needed to have shown the identical preparation method. The Applicants respectfully disagree with the Examiner's assessment. No further proofs should be required.

It first should be appreciated that the novelty of the subject invention does not reside in the particular type of polyacrylamide gel employed, but that, in view of that prior art which teaches against the use of polyacrylamide gel because of its association with toxic substance, e.g. acrylamide monomers, one skilled in the art would not have expected that a polyacrylamide gel, placed in a mammal, would make it possible to form a medium favorable for cultivating cells for a period of time sufficient for the cells to produce a biologically active substance, for example insulin, to treat a medical condition in said mammal, for example diabetes, and that the polyacrylamide gel inside the formed connective-tissue capsule would provide a protection from immune effects of the host organism.

Applicants also wish to draw the Examiner's attention to the second full paragraph on

page 4 of the English translation of the Russian language document previously submitted wherein it is disclosed that the use of the heating procedure to remove toxic monomers from the polymer produced eliminates the previously employed method of washing the polymer to remove the monomers. Therefore, the heating method disclosed in the Russian language patent was only an improvement of other prior art methods known for separating acrylamide monomers from polyacrylamide.

Additionally, Applicants submit herewith a copy of an English abstract of Chinese Patent CN1228447, published prior to Applicants' filing date, which discloses a process for making medical use polyacrylamide gel which includes washing, soaking and extraction after-treatments of the polymer, but no heating step(s) to remove undesirable monomer.

Also enclosed are copies of further documents showing that other methods for separating monomers from polyacrylamide were known to those skilled in the art prior to the application filing date.

An article entitled "Injectable hydrophilic polyacrylamide gel Formacryl and tissue reponse to its implantation", a copy of which is submitted herewith, provides on page 12 in the right hand column in the second full paragraph with respect to preparation of the polyacrylamide Formacryl, that "After the termination of the synthesis, the final product was washed up to remove monomers and the residual catalyst." (That article also sets out on page 20 that the use of Formacryl suggests a high degree of biocompatibility in view of the minimal inflammatory response produced.)

U.S. Pat. No. 4,898,824 discloses the use of a polyacrylamide gel composition for supporting biologically active substances. The examples refer to washing and gel filtration which presumably would remove monomers before use. GB 2114578 discloses a method of preparing polyacrylamide gel for medical applications, including nutrient media for growing microorganisms, artificial crystalline lenses, and elastic contact lenses. The steps of preparing the polymer include elution of the final product which should separate monomers from the polymer by size. U.S. Pat. No. 4,929,577 deals with a polyacrylamide-containing gel composition for dressing wounds. The patent states, in col. 4, lines 9-11, that "Post cure, when desired for removal of residual acrylamide monomer, is usually performed by placing the trays

in an oven for 3 hours at 60o (insert degree symbol)."

In view of the above, it is abundantly clear that methods for making and using medical grade polyacrylamide gel that can be used in the claimed invention were well-known to those of skill in the art as of the application filing date such that these methods need not be described in the present specification for the application to enable the claimed invention (see MPEP 2164.05(a)). Accordingly, it respectfully requested that the rejection of record be withdrawn and that the application proceed to allowance.

A petition and fee for extension of time for a further month is submitted herewith.

Respectfully Submitted,

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